



1614

THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Gregory S. HAMILTON et al.

Serial No. 09/920,017

Filed: August 2, 2001

For: **CARBOXYLIC ACIDS AND CARBOXYLIC ACID ISOSTERES OF  
N-HETEROCYCLIC COMPOUNDS**

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TRANSMITTAL LETTER

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Submitted herewith for filing in the U.S. Patent and  
Trademark Office are the following:

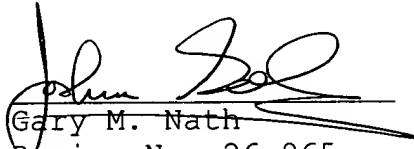
- 1) Transmittal Letter;
- 2) First Supplemental Information Disclosure Statement; and
- 3) PTO Form-1449.

The Commissioner is hereby specifically authorized to charge  
any fee deficiency or credit any overpayment in connection with  
this matter to our Deposit Account No. 14-0112.

Respectfully submitted,  
**NATH & ASSOCIATES PLLC**

Date: October 1, 2001  
NATH & ASSOCIATES, PLLC  
1030 15<sup>th</sup> Street, NW - 6<sup>th</sup> Floor  
Washington, D.C. 20005

By:

  
Gary M. Nath  
Regis. No. 26,965  
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Regis. No. 44,126  
Customer No. 20529



PATENT  
Attorney Docket No. AR762-XXA

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In re Application of

Gregory S. HAMILTON et al.

Serial No. 09/920,017

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For: **CARBOXYLIC ACIDS AND CARBOXYLIC ACID ISOSTERES OF  
N-HETEROCYCLIC COMPOUNDS**

**FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Pursuant to Applicants' duty of disclosure under 37 C.F.R. §§1.56 and 1.97-1.99, the documents listed on the attached Form PTO-1449 are being brought to the attention of the Examiner in charge of the captioned application. No fee is required for this submission because it is submitted within three months from the filing date or before a First Action on the Merits has been mailed by the U.S. Patent and Trademark Office. Copies of the documents are not attached, because a copy of each of the listed documents was previously submitted in the copending U.S. Patent Application Serial No. 09/453,571 filed, December 2, 1999.

The Examiner is respectfully requested to cite the documents listed on the attached Form PTO-1449 in the next Office Action. In so doing, the Examiner is respectfully requested to initial in the space adjacent to the listing of each document on the Form PTO-1449, and return a copy of the initialed Form PTO-1449 with the next communication to Applicants, to confirm that these

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If the Examiner has any questions or wishes to discuss this application, kindly telephone the undersigned attorney.

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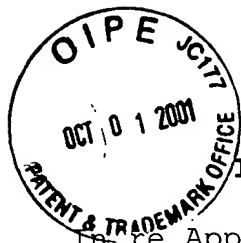
By: 

Gary M. Nath  
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GMN:TLJ:JBG:RAC / IDS.initial.wpd

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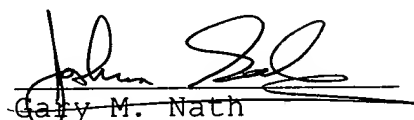
- 1) Transmittal Letter;
- 2) Second Supplemental Information Disclosure Statement; and
- 3) PTO Form-1449.

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~~Gary M. Nath~~  
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Attorney Docket No. AR762-1600/2900

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SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

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Washington, D.C. 20231

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This second supplemental IDS cites references which are relevant to the proviso species of claim 1. For the Examiner's convenience, a copy of the provisos from claim 1 follow wherein the relevant Form PTO 1449 reference numbers [e.g. **AC**, **BG**, etc.] are

documents have been considered by the Examiner and made of record in this application.

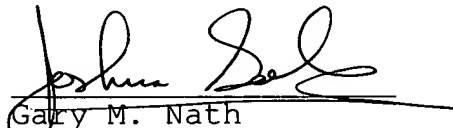
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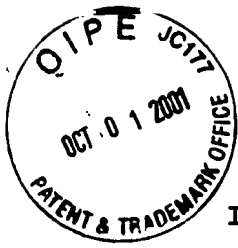
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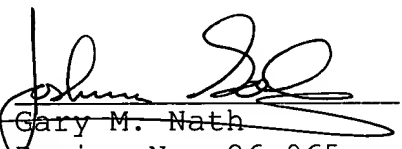
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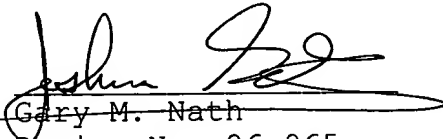
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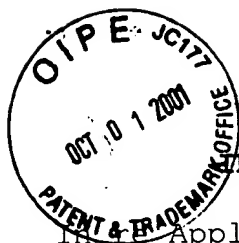
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Attorney Docket No. AR762-XXA



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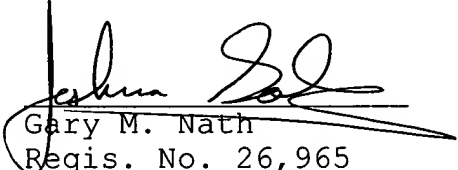
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GMN:TLJ:JBG:RAC / IDS.03.wpd

included in parentheses after the corresponding proviso species.

Proviso from claim 1:

A. provided that:

when  $n=1$ , and D is a bond, and  $R_2$  is COOH,

then  $R_1$  is not  $C_1$ - $C_9$  straight or branched chain alkyl [AA, AB,

AC, AD, AG, AI, AK, AL, AM, AN, AP, BA, BB, BC, BD, BE, BF,

BG, BH, BI, BN],  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_5$ - $C_7$

cycloalkyl,  $C_5$ - $C_7$  cycloalkenyl, phenylamine [BL, CB], 2-(3,4-dichlorophenyl)ethyl, hydroxy [AE, AF, AH, AJ, BJ, BM],

ethoxy [BK, CC], benzyl, or  $Ar_1$ , where  $Ar_1$  is 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl,

2-thienyl, 3-thienyl, 1-pyridyl, 2-pyridyl, 3-pyridyl, 4-

pyridyl, or phenyl [AO, BO], and wherein said alkyl, alkenyl,

cycloalkyl, cycloalkenyl, or  $Ar_1$  are optionally substituted

with one or more substituents selected from the group

consisting of hydrogen, halo, hydroxyl, nitro,

trifluoromethyl,  $C_1$ - $C_9$  straight or branched alkyl,  $C_2$ - $C_9$

straight or branched alkenyl,  $C_1$ - $C_4$  alkoxy,  $C_2$ - $C_4$  alkenyloxy,

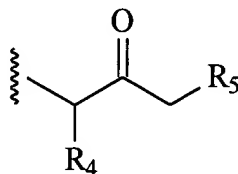
phenoxy, benzyloxy, COOH [CA], and amino; [This proviso also

removes matter claimed in applicant's co-pending U.S.

application No. 08/998,002.]

B. further provided that:

when  $n=1$ , and D is a bond, and  $R_2$  is the carboxylic acid isostere  $-\text{CONZ}(R^3)$ , and Z is hydrogen or  $C_1-C_6$  alkyl, and  $R^3$  is phenyl, or  $C_2-C_6$  straight or branched chain alkyl or alkenyl, wherein said alkyl is unsubstituted or substituted in one or more positions with  $\text{Ar}_2$  as identified below,  $C_3-C_8$  cycloalkyl, cycloalkyl connected by methyl or a  $C_2-C_6$  straight or branched alkyl or alkenyl chain,  $C_1-C_4$  alkyl ester, or  $\text{Ar}_3$  where  $\text{Ar}_3$  is selected from the group consisting of 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, having one to three substituents independently selected from the group consisting of hydrogen, halo, hydroxy, nitro, trifluoromethyl,  $C_1-C_6$  straight or branched alkenyl,  $C_1-C_4$  alkoxy,  $C_2-C_4$  alkenyloxy, phenoxy, benzyloxy, and amino; wherein said alkyl ester is optionally substituted with phenyl; or  $R^3$  is the fragment:



where  $R^4$  is selected from the group consisting of straight or branched chain  $C_1-C_8$  alkyl optionally substituted with  $C_3-C_8$  cycloalkyl, benzyl, or  $\text{Ar}_2$  as defined below, and where  $R_2$  is

**PATENT**

Attorney Docket No. AR762-XXA

COOZ or CONR<sup>6</sup>, where R<sup>6</sup> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> straight or branched alkyl, and C<sub>2</sub>-C<sub>6</sub> straight or branched alkenyl, and where R<sub>5</sub> is selected from the group consisting of phenyl, benzyl, C<sub>1</sub>-C<sub>6</sub> straight or branched alkyl, and C<sub>2</sub>-C<sub>6</sub> straight or branched alkenyl, where said alkyl or alkenyl is optionally substituted with phenyl; then R<sub>1</sub> is not C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl [EA, EB, EC, EM, FC, FD, FE, FG], C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, substituted thiophene [ED, EE, EH, EK], or C<sub>1</sub>-C<sub>4</sub> alkoxy [EG, EH, EJ, EK, EL, EN], wherein said alkyl or alkenyl is optionally substituted in one or more positions with C<sub>3</sub>-C<sub>8</sub> cycloalkyl [EI], C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, or Ar<sub>2</sub>, where Ar<sub>2</sub> is defined below, where said alkyl, alkenyl, cycloalkyl or cycloalkenyl groups may be optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkenyl, or hydroxy, and where Ar<sub>2</sub> is 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, having one to three substituents independently selected from the group consisting of hydrogen, halo, hydroxy, nitro, trifluoromethyl, C<sub>1</sub>-C<sub>6</sub> straight or branched alkyl or alkenyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>2</sub>-C<sub>4</sub> alkenyloxy, phenoxy, benzyloxy, and amino;

**[This proviso also removes matter claimed in applicant's**

**U.S. Patent No. 5,614,547, reference AH of the Supplemental**

**IDS]** .

C. further provided that:

when  $n=1$ , and X is O, and D is a bond, and  $R_2$  is  $-\text{CONH}_2$ ,  
then  $R_1$  is not methyl **[FB, FF]**, ethyl, isopropyl, isobutyl,  
isopentyl, 4-methylpentyl, indoyl, phenyl, or hydroxyphenyl;

D. further provided that:

when  $n=1$ , and X is O, and D is a bond, and  $R_2$  is cyano,  
then  $R_1$  is not methyl **[FM]**;

E. further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is  $-\text{CONZ}(R^3)$ ,  
and  $R_1$  is ethoxy,  
then  $R^3$  or Z is not halo-substituted phenyl **[FA]**;

F. further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is  $-\text{CONZ}(R^3)$ ,  
and  $R_1$  is substituted thiophene or tetrahydropyranoxy, or  
methoxy, then  $R^3$  or Z is not  $\text{C}_1\text{-C}_4$  alkyl ester substituted  
ethyl;

G. further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is  $-\text{CONZ}(R^3)$ ,  
and  $R_1$  is ethoxy,  
then  $R^3$  or Z is not 4-chlorophenyl **[FA]**;

H. further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is  $-\text{CONZ}(R^3)$ ,  
and  $R_1$  is cyclohexyl,  
then  $R^3$  or Z is not ethyl or propyl substituted with phenyl  
**[EI]**;

J. further provided that:

when D is  $\text{CH}_2$ ,  
then  $R_1$  is not  $-\text{OMe}$  **[FI, FK, FL]**,  $-\text{NHMe}$  or substituted  
 $-\text{NHcyclohexyl}$ ;

K. further provided that:

when D is  $\text{CH}_2$ , and  $R_2$  is  $-\text{OH}$   
then  $R_1$  is not phenyl **[FH]** or pyrrolidinemethanol;

L. further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is  $-\text{COOH}$ ,  
then  $R_1$  is not methyl, tert-butyl **[CE]**, 1,1-dimethyl-2-methyl-  
propyl **[CE, DE, DF, DH, DM]**, 1,1-dimethylpropyl **[CF, CG, CK,**  
**CM, DE, DF, DH, DM, DN]**, methoxy **[CH, CI, CJ, CL, CN, DA, DG,**

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**DI**], ethoxy [**DK,DO**], phenyl [**CH, CJ, CN, DA, DG, DI**],  
tetrahydropyranoxy substituted C<sub>4</sub>-C<sub>6</sub> alkyl [**DE, DF, DH, DM**],  
1-methyl-1-methoxyamide, 1-methylcyclohexyl [**CE**], 3-iodophenyl  
[**CO, DL**],  
3-methyl ester cyclopentyl [**DC**], 1,1-dimethyl-6-phenyl-hex-  
3,5-dioxy, or trimethoxyphenyl [**CD, DB, DJ**].

The Examiner's attention is also drawn to the following IDS references containing biological information that the Examiner may find relevant for reviewing the subject matter of the present invention.

**BF, EF** - glaucoma

**CL** - neuronal damage

**CI** - growth of neurites

- neuronal damage

**EB** - neurite outgrowth

- Parkinson's disease in mice

**ED** - neuronal growth

- neuronal disorders

**EE** - nerve growth

- Alzheimer's disease; parkinsonism

**EA** - inhibitors of rotamase enzyme

**EO, FJ** - anti-amnesic



**PATENT**

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Additional references are disclosed herein which refer to species that are to be excluded from the scope of claim 1 by amendment. These additional references are **DC, DD, EF, EO, and FJ**.

The Examiner is respectfully requested to cite the documents listed on the attached Form PTO-1449 in the next Office Action. In doing so, the Examiner is respectfully requested to initial in the space adjacent to the listing of each document on the Form PTO-1449, and return a copy of the initialed Form PTO-1449 with the next communication to Applicants, to confirm that these documents have been considered by the Examiner and made of record in this application.


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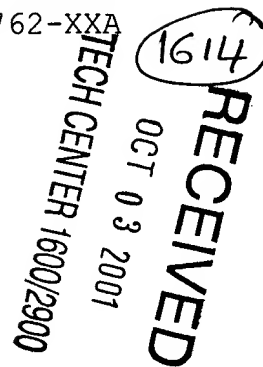
Date: October 1, 2001  
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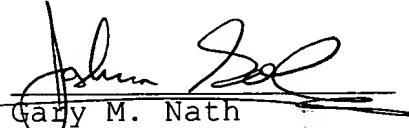
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Washington, D.C. 20231

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Pursuant to Applicants' duty of disclosure under 37 C.F.R. §§1.56 and 1.97-1.99, the documents listed on the attached Form PTO-1449 are being brought to the attention of the Examiner in charge of the captioned application. No fee is required for this submission because it is submitted within three months from the filing date or before a First Action on the Merits has been mailed by the U.S. Patent and Trademark Office. Copies of the documents are not attached, because a copy of each of the listed documents was previously submitted in the copending U.S. Patent Application Serial No. 09/453,571, filed December 2, 1999.

The Examiner is respectfully requested to cite the documents listed on the attached Form PTO-1449 in the next Office Action. In so doing, the Examiner is respectfully requested to initial in the space adjacent to the listing of each document on the Form PTO-1449, and return a copy of the initialed Form PTO-1449 with the next communication to Applicants, to confirm that these

documents have been considered by the Examiner and made of record in this application.

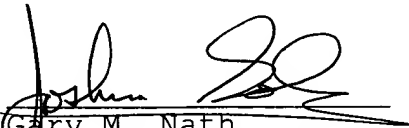
If the Examiner has any questions or wishes to discuss this application, kindly telephone the undersigned attorney.

Respectfully submitted,

**NATH & ASSOCIATES PLLC**

Date: October 1, 2001  
NATH & ASSOCIATES, PLLC  
1030 15<sup>th</sup> Street, NW - 6<sup>th</sup> Floor  
Washington, D.C. 20005

By:

  
Gary M. Nath  
Regis. No. 26,965  
Joshua B. Goldberg  
Regis. No. 44,126  
Customer No. 20529

GMN:TLJ:JBG:RAC / IDS.04.wpd



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

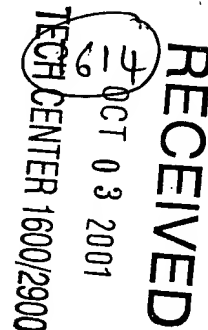
In re Application of

Gregory S. HAMILTON et al.

Serial No. 09/920,017

Filed: August 2, 2001

For: **CARBOXYLIC ACIDS AND CARBOXYLIC ACID ISOSTERES OF  
N-HETEROCYCLIC COMPOUNDS**



**TRANSMITTAL LETTER**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Submitted herewith for filing in the U.S. Patent and  
Trademark Office are the following:

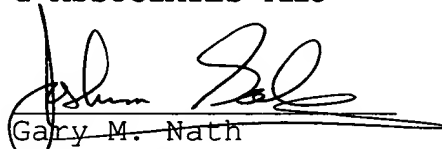
- 1) Transmittal Letter;
- 2) Fifth Supplemental Information Disclosure Statement; and
- 3) PTO Form-1449.

The Commissioner is hereby specifically authorized to charge  
any fee deficiency or credit any overpayment in connection with  
this matter to our Deposit Account No. 14-0112.

Respectfully submitted,  
**NATH & ASSOCIATES PLLC**

Date: October 1, 2001  
NATH & ASSOCIATES, PLLC  
1030 15<sup>th</sup> Street, NW - 6<sup>th</sup> Floor  
Washington, D.C. 20005

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Gary M. Nath  
Regis. No. 26,965  
Joshua B. Goldberg  
Regis. No. 44,126  
Customer No. 20529



PATENT  
Attorney Packet No. AR762-XXA

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Gregory S. HAMILTON et al.

Serial No. 09/920,017

Filed: August 2, 2001

For: **CARBOXYLIC ACIDS AND CARBOXYLIC ACID ISOSTERES OF  
N-HETEROCYCLIC COMPOUNDS**

**FIFTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Pursuant to Applicants' duty of disclosure under 37 C.F.R. §§1.56 and 1.97-1.99, the documents listed on the attached Form PTO-1449 are being brought to the attention of the Examiner in charge of the captioned application. No fee is required for this submission because it is submitted within three months from the filing date or before a First Action on the Merits has been mailed by the U.S. Patent and Trademark Office. Copies of the documents are not attached, because a copy of each of the listed documents was previously submitted in the copending U.S. Patent Application Serial No. 09/453,571 filed December 2, 1999.

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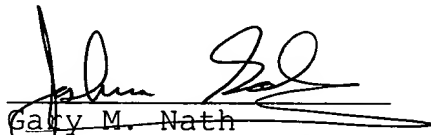
Respectfully submitted,

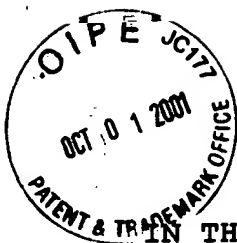
**NATH & ASSOCIATES PLLC**

Date: October 1, 2001  
NATH & ASSOCIATES, PLLC  
1030 15<sup>th</sup> Street, NW - 6<sup>th</sup> Floor  
Washington, D.C. 20005

GMN:TLJ:JBG:RAC / IDS.05.wpd

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PATENT  
Attorneyocket No. AR762-XXA

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Gregory S. HAMILTON et al.

Serial No. 09/920,017

Filed: August 2, 2001

For: **CARBOXYLIC ACIDS AND CARBOXYLIC ACID ISOSTERES OF  
N-HETEROCYCLIC COMPOUNDS**

**SIXTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Pursuant to Applicants' duty of disclosure under 37 C.F.R. §§1.56 and 1.97-1.99, the documents listed on the attached Form PTO-1449 are being brought to the attention of the Examiner in charge of the captioned application. No fee is required for this submission because it is submitted within three months from the filing date or before a First Action on the Merits has been mailed by the U.S. Patent and Trademark Office. Copies of the documents are not attached, because a copy of each of the listed documents was previously submitted in the copending U.S. Patent Application Serial No. 09/453,571 filed December 2, 1999.

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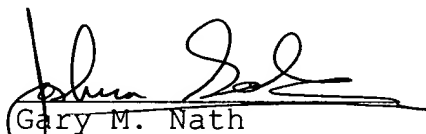
If the Examiner has any questions or wishes to discuss this application, kindly telephone the undersigned attorney.

Respectfully submitted,

**NATH & ASSOCIATES PLLC**

Date: October 1, 2001  
NATH & ASSOCIATES, PLLC  
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By:

  
Gary M. Nath  
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Joshua B. Goldberg  
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GMN:TLJ:JBG:RAC / IDS.06.wpd